to TBP-II. By this method, one can determine over-production or under-production of TBP-II by comparing the level of TBP-II found in such an assay with the normal levels of TBP-II found in the body fluids of healthy subjects.

The examiner states that, upon reconsideration of applicant's amended claims, it appears that the effective priority date of the instant claims is the filing date of priority application 07/524,263. However, the examiner incorrectly states that the filing date of this application is May 16, 1992. It can be seen from the Official Filing Receipt of record in this case as well as in the Declaration of record in this case, that application 07/524,263 was filed on May 16, 1990. The examiner is requested to confirm this with PTO records. Accordingly, we will assume this was a typographical error and that the effective date that the examiner has agreed is available to the present claims is May 16, 1990.

The examiner states that he disagrees that applicant is entitled to the effective filing date of foreign priority application IL 091229 of August 6, 1989. Applicant disagrees with the examiner's conclusion that applicant is not entitled to the effective date of Israeli application filed August 6, 1989. Nevertheless, as this issue is not critical in order to respond to the present office action, applicant will reserve appropriate

arguments and explanations until such time that it is necessary to do so in light of an intervening reference.

Claims 1 and 6 have been rejected as being anticipated by Brockhaus (EP 0334165). The examiner states that the Brockhaus European patent teaches antibodies to TNF receptor and their use as diagnostic tools for the determination of TNF receptors on the cell surface and in soluble form. The examiner states that, while the prior art does not disclose the terminology TBP-II or SEQ ID N0: 3, *per se*, it appears that the prior art and the instant claims are drawn to the same p75 tumor necrosis factor receptors. This rejection is respectively traversed.

Contrary to the examiner's statement, there is nothing in the Brockhaus European patent that would suggest that the antibodies thereof are directed against the p75 tumor necrosis factor receptor. Indeed, a subsequent publication of the same inventors and others teaches that the antibodies in the Brockhaus European patent are directed to TBP-I, or the p55 tumor necrosis factor receptor. Submitted herewith is Brockhaus et al., "Identification of Two Types of Tumor Necrosis Factor Receptors on Human Cell Lines by Monoclonal Antibodies," *Proc. Natl. Acad. Sci. USA*, 87:3127-3131 (1990)). As can be seen from the third paragraph of column 5 of the Brockhaus European patent, the antibodies of that patent are those referred to as

htr-1 to htr-9. It is clear from the examples of the Brockhaus European patent that all of these antibodies were obtained from antigens appearing on HL-60 cells. This is confirmed by the first sentence of the results section at page 3128 of the Brockhaus *PNAS* publication, which states that htr antibodies (htr1-9) were obtained with immunogen purified from HL-60 cells.

Of particular interest is the sentence bridging pages 3130-3131 of the Brockhaus PNAS publication, where it states that the htr antibodies detect the 55/50-kDa type-B TNF-binding protein. In the previous sentence, this publication states that the antibodies are non-cross reacting. It is well known today that the p55 tumor necrosis factor receptor is a distinctly different receptor from the p75 tumor necrosis factor receptor. The present invention is directed to the p75 tumor necrosis factor receptor, the soluble extracelluar portion of which is now known as TBP-II. Thus, the examiner is incorrect in stating that the antibodies of the Brockhaus European patent are directed to the same p75 TNF receptor as are the presently claimed antibodies. The evidence submitted herewith establishes that the antibodies of the Brockhaus European patent are directed to the structurally distinct p55 TNF receptor and thus their use in an immunoassay is necessarily different from the use of the distinctly different antibodies of the present claims.

Accordingly, as none of the antibodies of the Brockhaus European patent can specifically recognize and bind TBP-II, none of the present claims can possibly be anticipated by the Brockhaus European patent. Reconsideration and withdrawal of this rejection are therefore respectively urged.

Claims 1 and 6 have been rejected under 35 U.S.C. §102(a) as being unpatentable over the Brockhaus European patent in view of Wolpe. The examiner cites Wolpe for the obviousness of comparing the over-production and under-production of TBP-II in an immunoassay to detect tumor necrosis binding proteins. This rejection is respectively traversed.

Wolpe adds nothing to the deficiencies of the Brockhaus Eurpoean patent discussed above, as Wolpe does not disclose antibodies to TBP-II. As discussed above, the Brockhaus European patent teaches only antibodies to TBP-I. Accordingly, this rejection must be withdrawn for the same reasons as discussed above with respect to the anticipation rejection over the Brockhaus European patent. Reconsideration of withdrawal of this rejection are therefore respectively urged.

Claims 1 and 6 have been rejected under 35 U.S.C. §103(a) as being unpatentable over the Brockhaus European patent in view of Wolpe and further in view of the Brockhaus US Patent 5,610,279. The examiner states that the Brockhaus US patent

teaches antibodies to TNF receptor including antibodies to TBP-II and their use as diagnostic tools for the determination of TNF receptors on the cell surface and in soluble forms. This rejection is respectively traversed.

The examiner has conceded that applicant is entitled to the effective filing date of US Application No. 07/524,263. This filing date is May 16, 1990. The earliest date as a reference for the Brockhaus U.S. patent is September 10, 1990. Accordingly, it is not available as a reference. Reconsideration of withdrawal of this rejection are therefore also respectively urged.

It is submitted that all of the claims now present in the case clearly define over the references of record and fully comply with 35 U. S. C. § 112. Reconsideration and allowance are therefore earnestly solicited.

Respectfully submitted,

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